REMARKS

Formal Matters

The claims have been amended simply for clarification. Perhaps, "carbohydrate composition" is not sufficiently specific; as what is supplied is a polysaccharide degrading enzyme, what is altered is the polysaccharide/saccharide content of the plant.

Applicants appreciate the consideration of the Declaration submitted by Dr. J. Pen and entry of the amendment filed 12 June 2000. Applicants note the necessity to comply with the sequence rules and a Sequence Listing in compliance with these rules is submitted along with this response.

The Rejection

The sole basis for rejection is under 35 U.S.C. § 112, first paragraph, on the basis of an asserted lack of enablement. There is no assertion of any lack of written description.

First, as applicants are certain the Office is aware, the burden is on the Office to provide documentation or sound scientific reasoning to support any doubt the teachings of the specification. See, for example, *In re Marzocchi*, 439 F2d 220, 169 USPQ 367 (CCPA 1971). Unless such documentation and/or scientific reasoning are adduced, the statements made in the specification are to be taken at face value.

Taken as a whole, the application simply discloses that by providing to a plant, through genetic modification, a nucleotide sequence encoding a polysaccharide degrading microbial enzyme along with suitable regulatory and targeting sequences, the carbohydrate composition of the plant or plant organ can be altered. This does not seem inherently incredible. Here, the basis for this rejection appears to be only the personal opinion of the Examiner that the statements made in the specification are untrue. For example, the statement on page 3, lines 8-13 is evidently doubted as is the statement on page 5, lines 11-17. The scope, based on the nature of the enzymes which are listed on page 6 beginning at line 22 and on the nature of the plant as suggested on page 8 beginning at line 25 is also questioned.

Initially, in support of this position of doubt, the Examiner complained that various techniques for enhancing the expression of microbial genes in plants were not described in the specification. According to the sworn testimony of Dr. Pen, the techniques postulated by the Examiner to be necessary for success are either in fact not necessary or are sufficiently well-known to the ordinary artisan so that no instruction in the specification would be needed as to

how to perform them. Apparently, this aspect of the basis for doubting the specification has been overcome. For this, applicants are appreciative.

Now, the Office expresses doubt that "the inserted glucanase of any microbial origin will be expressed in any plant species to produce glucanase that is functional in the plant with the ability to modify carbohydrate composition." The apparent logic behind this is not directed to failure to produce functional glucanase, but rather that the glucanase expressed will not have any effect on carbohydrate composition because carbohydrate metabolism is complicated, because a "large number of enzymes are involved in carbohydrate composition in any plant cell" and there are many "known pathways that are involved in regulating carbohydrate composition."

Maybe so. But it is not seen how the complexity of carbohydrate metabolism is sufficient to render incredible the assertion by applicants that by inserting a polysaccharide degrading enzyme, polysaccharides will in fact be degraded and thus the polysaccharide content will be altered. This does not strain belief in the least.

The Office goes on to comment that "none of the descriptions provided in the specification nor the references of the prior art were shown that the expression of a single enzyme is capable of modulating a complex subject matter such as carbohydrate."

This is clearly untrue.

Cited on page 2 of the specification at line 21 is PCT publication WO 89/12386 which describes a modification of carbohydrate content by expression of sucrase or levan sucrase. And the specification has working examples: the saccharide content of tobacco leaves is altered by the introduction of α-amylase into tobacco plants as shown in Table 1 on page 21. Example 8 states specifically that "transgenic plants expressing α-amylase contain demonstrably less starch in their leaves than control plants." And Example 12 states on page 28, lines 14-17 that "tubers of transgenic potatoes expressing both enzymes (glucoamylase and α-amylase) are analyzed for the presence of soluble sugars by HPLC. A higher content of soluble sugars is found in transgenic tubers as compared to control plants."

So it just isn't true that none of the descriptions provided in the specification or references show that expression of a single enzyme is capable of modulating carbohydrate. And it certainly is not true that the enzymes described in the specification, α-amylase and glucoamylase, were not described to modulate carbohydrate composition in any plant "to the extent as claimed in the instant invention." To what extent is this claimed in the instant

invention? The claims merely require modifying the carbohydrate composition. No extent is mentioned.

The Examiner goes on to state that the specification doesn't teach that α-amylase or glucoamylase have characteristics associated with glucanase such as molecular weight, amino acid composition, N-terminal sequence, etc. In the first place, glucoamylase and α-amylases are glucanases. The undersigned is uncertain whether they are endoglucanases; however, that doesn't matter. It has been error all along to restrict the claims to endoglucanases. This error was elaborated in gory detail in the response mailed 27 August 1998 to the restriction requirement. It was there pointed out that it is the glucanase activity that is significant, not whether this is an endoglucanase, a 1,4 linkage cleaving glucanase, a 1,3 linkage cleaving glucanase, or whether the glucanase cleaves α or β linkages. The arbitrary nature of the classification apparently adopted by the Office was pointed out, but this was ignored in favor of characteristics totally irrelevant to the invention such as molecular weight, N-terminal sequence, amino acid composition, etc.

The essential features of the invention are thus obscured by the restriction requirement made on a basis totally irrelevant to the nature of the invention. The explanation for this requirement relates to structural characteristics, when it is the functional characteristics of the enzymes that matter to the method claims at issue.

All of the foregoing is to say that there is adequate proof that glucanases in general, including endoglucanases, are capable of modifying the polysaccharide/saccharide content of plants when microbial glucanases are expressed therein.

In response to the interpretation of Kossmann provided by the Office - that the document is cited to show that carbohydrate metabolism is "highly complex and incompletely understood" applicants point out that the present invention is not itself all that complicated. It is not necessary to understand all the complexities of carbohydrate metabolism to understand that inserting an enzyme that degrades polysaccharides will probably degrade polysaccharides and thus change the polysaccharide/saccharide content. Kossmann does not teach to the contrary. All that Kossmann demonstrated was that the absence of one enzyme which was known to synthesize starch failed to result in enhanced starch content. The only thing that was measured was starch. No other carbohydrates, such as sucrose, glucose, or other carbohydrates were measured. Therefore, it cannot be said the Kossmann teaches generally that inhibiting the production of starch synthase fails to change the carbohydrate content.

The statement that glucose itself is not available for oxidation without phosphorylation seems completely irrelevant to the issues here.

Respectfully, then, applicants believe that the Office has failed to establish such a "high degree of unpredictability" that the statements of the applications should be doubted and the working examples considered unrepresentative.

Applicants further note that the asserted unpredictability relating to the complexity of the metabolism of glucose in plants seems irrelevant to claims 54-57 which are directed simply to a DNA expression cassette, a vector containing it and plants and bacterial strains containing it.

CONCLUSION

Applicants submit that the only documentation provided in support of the rejection based on asserted non-enablement is the article by Kossmann, now said to be provided only for its teaching that carbohydrate metabolism is complex and not completely understood. This may be true, but it does not make incredible applicants' invention which is based on altering the ability of plants to degrade polysaccharides so as to change the balance between polysaccharides and saccharides. While there is no legal requirement to provide working examples to demonstrate operability when the invention is not inherently incredible, applicants have provided three such working examples in three different types of plants. Accordingly, it is believed that the rejection based on doubt of the teachings of the specification may properly be withdrawn and all pending claims, claims 1, 27-28, 42, 48, 51 and 54-58 be passed to issue.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 261922003302. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

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EXHIBIT A. - VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Thrice amended) A method for modifying the [carbohydrate] polysaccharide/saccharide composition of a plant or plant organ, wherein said method comprises growing a transformed transgenic plant containing a vector or recombinant expression construct encoding a microbial endo-glucanase operably linked to a regulatory or leader sequence under conditions wherein said glucanase is expressed and the carbohydrate composition of said plant or plant organ is modified by the expressed glucanase and said regulatory sequence is selected from the group consisting of

a) a regulatory sequence that directs expression of said enzyme-encoding nucleotide sequence at a selected stage of development or maturity of the transgenic plant or plant organ;

b) a regulatory sequence comprising a 35S CaMV promoter; and

c) a regulatory sequence directs tissue-specific expression of said enzyme-encoding nucleotide sequence in a plant; and wherein said leader sequence targets the expressed endo-glucanase to the [carbohydrate] polysaccharide/saccharide material contained in a cellular compartment or organelle.

58. (Thrice amended) A stably transformed, transgenic plant or plant organ, characterized in that said plant or plant organ contains a endo-glucanase modified [carbohydrate] polysaccharide/saccharide composition contained in a cellular compartment or organelle, said plant or plant organ being made by the method of claim 1.